REMARKS

I. Status of the Claims

Claims 1, 3, 12-17, and 53-55 are pending. Claims 2, 4-11, and 18-52 are canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to the canceled subject matter.

Claim 1 is amended to incorporate the subject matter of claims 6 and 8.

Claims 54 and 55 are added. Claim 54 is an independent claim drawn to the combined subject matter of claims 1 and 6. Claim 55 is an independent claim drawn to the combined subject matter of claims 1 and 7.

Since these amendments introduce no new matter, Applicants respectfully request that they be entered into the record.

II. The anticipation rejections over Garcon and MacFarlan are defeated because neither reference teaches an antigen with increased positive charge

Claims 1, 3, 6, and 12-17 are rejected as allegedly anticipated by WO 96/33739 ("Garcon"). Claims 1, 3, 7, and 12-13 likewise are rejected over WO 98/36772 ("MacFarlan").

Not rejected over Garcon is Claim 8, which recites a combination of an organic complex with increased negative charge and an antigen with increased positive charge. By the present amendment of claim 1 to incorporate the salient recitations of claim 8, Applicants submit that they have overcome the rejection based on Garcon.

Rejected over MacFarlan, claim 7 qualifies base claim 1 in terms of an antigen that had been modified so as to have an increased positive charge. MacFarlan actually does not teach a composition with an organic complex with a modified (increased) negative charge. Since MacFarlan does not teach every limitation of the claimed invention, the reference is not anticipatory and the rejection should be withdrawn.

III. The skilled artisan would not have added Garcon's negatively charged lipid to MacFarland's uncharged complex, since that would have destroyed MacFarland's chelation-based polypeptide complex system

Claims 6, 8, and 53 are rejected over MacFarlan in view of Garcon. The Office states that Applicants' arguments of July 27, 2006, "are not persuasive for the reason(s) set forth in the paragraphs following paragraphs 4 and 5 of *this* office action . . . Hence, the rejection is maintained" (page 5; emphasis added). In fact, paragraph 6 of the present action merely states that claims 6, 8 and 53 "are rejected" and presents an abbreviated summary of Applicants' position that the claims are not obvious.

Accordingly, the Office has not met its burden of coming forward with a *prima facie* case under Section 103. In other words, the Office has articulated no reason that complies with its obligations under *Graham v. John Deere Co.*, 383 U.S. 1 (1966), and *KSR International Co. v. Teleflex Inc. et al.*, 127 S.Ct. 1727 (2007), that it *at the very least* "identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." Applicants submit, therefore, that the Office has not established a *prima facie case* of obviousness.

Their position in this regard is unaffected by the Office's comments at pages 10 and 11 of the Office Action dated March 28, 2006. There the Office stated that "MacFarland et al. does not teach the enhancement of the negative charge of the organic complex," but that Garcon remedies this because Garcon adds negatively charged lipid "to increase the stability of liposomes, which is an organic complex." According to the Office, it therefore "would have been *prima facie* obvious . . . to add a negatively charged lipid to the organic carrier of MacFarland et al. [because the skilled person] would have been motivated to do so to enhance the stability of the organic carrier . . . the addition of a negatively charged lipid into the organic carrier would result in the enhancement of the carrier's overall negative charge." *Id.*

To the contrary, as Applicants have explained elsewhere in the record, the very essence of MacFarland is an ***uncharged*** immunostimulating complex matrix. MacFarland's system relies exclusively on chelation, whereby a coordination complex is formed by the bonding of a ligand to a central metal atom by coordinate covalent bonding. Thus,

MacFarland's composition includes a metal-chelating moiety that binds a polypeptide that has at least one chelating amino acid sequence via a suitable metal ion. In MacFarlan's system, metal ions such as nickel ions, are electrostatically bound to a chelating moiety, like iminodiacetic acid, which fully neutralizes the charge on the metal ions but leaves coordination sites available on the metal for electron sharing to occur

Coordination complexes therefore ***differ*** from electrostatic complexes because heavy metal ions are essential to MacFarland's coordination complex, whilst they are unnecessary and irrelevant to electrostatic interactions, and because the ligand and receptor in a coordination complex are joined by covalent bonds – the antithesis of an electrostatic interaction. MacFarland's system "attaches" a desired polynucleotide to the complex via chelation, whereby a metal ion links the two elements together.

Informed by these principals, which stand uncontroverted on the record, the person of ordinary skill in the art would **not** have considered adding a negatively charged lipid "to the organic carrier of MacFarland," in order to "enhance the stability of the organic carrier," because the negatively charged lipid would utterly destroy MacFarland's ***uncharged*** chelation-based system. Indeed, the skilled artisan would have predicted MacFarland's polypeptide, if it comprised any positively charged amino acid residues, to be attracted electrostatically to the negatively charged lipid, which would completely disrupt the intended chelation-specific bonding process that MacFarland requires for the desired complex.

Accordingly, the artisan not only would have lacked motivation to add a negative charge lipid to MacFarland's complex but she also would have had ***no*** reasonable expectation of success that such an addition would enhance the stability of the organic complex. Rather, the artisan would have expected disruption or destruction for MacFarland's chelated polypeptide complex, consequent to the addition of Garcon's negatively charged lipid.

Furthermore, no reasonable permutation of teachings gleaned from MacFarland and Garcon would have informed the person of ordinary skill about increasing the charges of an antigen or complex beyond its natural ionic charge, such that a complex is more negatively

charged and an antigen is more positively charged than normal, promoting their electrostatic interaction.

For at least these reasons, the Office has not established a *prima facie* case of obviousness. Applicants therefore respectfully request withdrawal of this obviousness rejection.

IV. Double patenting

Claims 1, 3, 6-8, 12-17 and 53 remain provisionally rejected on grounds of obviousness-type double patenting over claims of copending U.S. application serial No. 10/622,470. Because the rejection is provisional, Applicants still defer any argument or "corrective" action until the Office allows claims in one of the copending applications.

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Applicants request favorable reconsideration of the application. If the Examiner believes that an interview would advance prosecution, she is invited to contact the undersigned directly.

Respectfully submitted,

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The Commissioner is authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, Applicants hereby petition for such extensions under 37 CFR §1.136 and authorize payment of the relevant fee(s) from the deposit account.